Original Article

Effect of dexmedetomidine infusion on hemodynamic responses in microsurgery of larynx

Shakuntala Basantwani, Mayuresh Patil, Balasaheb Govardhane, Jyoti Magar, Bharati Tendolkar

Department of Anaesthesiology, LTMMC and LTMGH, Sion, Mumbai, Maharashtra, India

Abstract

Background and Aims: Microlaryngeal surgery is a frequently performed ear, nose, and throat procedure used to diagnose and treat laryngeal disorders. Suspension laryngoscopy causes prolonged stimulation of the deep pressure receptors of the larynx leading to adverse circulatory responses and consequently cardiac complications. In this study, dexmedetomidine infusion was used to assess its effectiveness for attenuation of this hemodynamic stress response.

Material and Methods: Sixty patients undergoing elective microlaryngeal surgery randomly received either dexmedetomidine 1 µg/kg over 10 min followed by continuous infusion of 0.5 µg/kg (Group D) or normal saline infusion at the same rate (Group P) till the end of surgery. Anesthesia in all patients was induced with propofol, succinylcholine to facilitate endotracheal intubation after premedication with fentanyl 2 µg/kg and glycopyrrolate. Intraoperative, vital parameters were maintained within 20% of baseline with rescue analgesic fentanyl 1 µg/kg and subsequently with propofol boluses up to 1 mg/kg. The percentage of patients and the total amount of intraoperative fentanyl and propofol required in each group were recorded. Sedation score at 10 minutes postextubation was assessed by Ramsay sedation score.

Results: Intraoperative heart rate and mean arterial pressure in Group D were lower than the baseline values and the corresponding values in Group P ($P < 0.05$). The percentage of patients requiring rescue fentanyl and propofol was higher in Group P than Group D (36.6% and 30% vs. 6.6% and 3.3% $P = 0.01$). Recovery scores were better in dexmedetomidine group.

Conclusion: Dexmedetomidine infusion attenuates the hemodynamic stress response during laryngoscopy, intubation, and microlaryngeal surgery and is associated better recovery profile.

Keywords: Anesthesia, dexmedetomidine, hemodynamic response, intubation, microlaryngoscopy, suspension laryngoscopy

Introduction

Manipulation of larynx during laryngoscopy and tracheal intubation leads to hemodynamic and cardiovascular responses secondary to release of catecholamines.[1] Similar responses, more intense and prolonged than laryngoscopy and endotracheal intubation are encountered during microlaryngoscopic procedures due to a longer duration of suspension laryngoscopy (20–30 min as against 15–30 s) and surgical manipulation. The adverse circulatory changes occurring throughout the procedure can be of sufficient magnitude to induce myocardial ischemia, cardiac dysrhythmias, and cerebrovascular accidents in elderly patients with poor cardiopulmonary reserve.[2] Mitigating the perioperative stress response with a drug that effectively suppresses these obnoxious stress stimuli while handling the laryngeal aperture and vocal cords along with maintenance of adequate depth of anesthesia without compromising oxygenation and ventilation and with a rapid recovery profile is required.

Address for correspondence: Dr. Shakuntala N. Basantwani,
404, Paloma A Wing, Hiranandani Estate,
Ghodbunder Road Patlipada, Thane (W), Maharashtra, India.
E-mail: drbasantwani@hotmail.com

Dexmedetomidine, a highly selective, specific, and potent α2 adrenergic receptor agonist, owing to its central sympatholytic, anxiolytic properties are known to be effective in suppressing stress response to intubation.[3] Hence, we hypothesized and investigated the effects of dexmedetomidine infusion on hemodynamic response in patients undergoing microlaryngoscopy (MLScopy) under general anesthesia. The primary aim was to maintain hemodynamics within 20% of baseline values during critical incidences such as laryngoscopy, endotracheal intubation, and MLScopy. The intraoperative requirement of fentanyl as rescue analgesic and propofol as an anesthetic to maintain the hemodynamics within the range of 20% baseline values was the secondary endpoint.

Material and Methods

This prospective, randomized, placebo-controlled, double-blind study was undertaken after institutional ethics committee approval. Sixty patients of either sex, having the American Society of Anesthesiologists (ASA) Grade I to III, aged between 18 and 60 years, undergoing elective microlaryngeal surgery under general anesthesia were included and written informed consent was obtained from all the participants. Hemodynamically unstable patients, patients with Ischemic heart disease, and those having left bundle-branch block or atrioventricular block more than first degree were excluded from the study. A computer-generated randomization table was used to assign each patient to either Group "P" or Group "D." Randomly allocated coded syringes containing either normal saline or dexmedetomidine 4 μg/ml (200 μg diluted in 50 ml normal saline) were prepared by an anesthesiologist not involved in either conducting the case, data recording or for monitoring during intra- and post-operative periods. After confirming adequate nil per oral status, patients were wheeled in the operation theater, and baseline heart rate (HR), electrocardiogram (ECG), arterial blood pressure (BP), oxygen saturation were recorded.

An intravenous access was secured with 20-gauge cannula for infusion of intravenous fluid, and Ringer lactate solution was infused at 2–3 ml/kg/h. An additional intravenous access was secured for infusion of study drug after premedication with glycopyrrolate 0.004 mg/kg and fentanyl 2 μg/kg. Group D received intravenous dexmedetomidine 1 μg/kg over 10 min followed by continuous infusion of 0.5 μg/kg/h. Group P received normal saline infusion at the same rate. All the patients received oxygen through nasal prongs at 2 l/min.

Fifteen minutes later, induction of anesthesia was carried out using propofol (2–2.5 mg/kg) till loss of eyelash reflex. Endotracheal intubation was facilitated by muscle relaxant succinylcholine (1.5 mg/kg). Under direct laryngoscopic vision, tracheal intubation was done with MLScopy tube of appropriate size 5 and 5.5. Anesthesia was maintained with 50% nitrous oxide in oxygen, and 2.0% end-tidal sevoflurane on close circuit with attached capnometer and ventilation was adjusted to maintain end-tidal CO_2 at 34–45 mmHg. Loading (0.5 mg/kg) and supplemental doses of atracurium 0.1 mg/kg were administered to provide immobile vocal cords. Suspension laryngoscope was fixed when HR and mean BP (MBP) returned to baseline values. Hemodynamic parameters, i.e., MBP, HR was recorded at specific time points, i.e., premedication, later every 2 min during loading dose infusion of study drugs and then at induction, laryngoscopy and intubation and thereafter at regular interval of 5 min throughout the surgical procedure. HR and MBP were maintained within 20% of baseline values. Fentanyl 1 μg/kg and later bolus doses of propofol up to1 mg/kg were used to maintain the hemodynamics. Number of patients requiring fentanyl as rescue analgesic and anesthetic propofol and their total dose required in each group was recorded. Hypotension (fall in systolic BP >20%) was treated with fluids and ephedrine hydrochloride if required. Bradycardia, i.e., HR <45 on two consecutive readings was treated with atropine sulfate. The infusion of study drugs and sevoflurane were continued till the removal of suspension laryngoscope. All patients received dexamethasone 0.1 mg/kg and ondansetron 4 mg. On completion of surgery, residual neuromuscular blockade was reversed using glycopyrrolate 0.008 mg/kg and neostigmine, 0.06 mg/kg. Tracheal extubation was performed after application of 4% lignocaine spray and excluding cord edema when patients were able to respond to simple verbal commands. Sedation score was assessed 10 min' postextubation and was shifted to the postanesthesia care unit (PACU) after complete clinical recovery where they received nasal O_2 supplementation, and were monitored for hemodynamic parameters, adverse events if any every 30 min for 2 h' till transferred to the surgical ward.

Statistical analysis

Data analysis was done with the help of SPSS version 15 (SPSS Inc., Chicago,USA). Demographic data were compared with the help of unpaired *t*-test and Fisher's exact test. Hemodynamic variables and various time intervals were analyzed using a unpaired *t*-test for intergroup analysis and paired *t*-test for intragroup analysis. Mann–Whitney U-test was used for data which were not distributed evenly. $P < 0.05$ was considered statistically significant.

The sample size calculation was done using the method described by Dupont and Plummer (1990) for continuous response measures in two independent groups according to the previous study.[4] Twenty-nine experimental and 29 control

subjects needed to be studied to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) 0.9. The type I error is 0.05 (α). Hence, sixty adult patients were included in the present study.

Results

Statistically, no difference in the patient characteristics and surgical data were detected between the groups [Table 1]. Laser excision of laryngeal mass was performed in 25% patients whereas 75% of patients underwent diagnostic scopy [Figure 1].

Baseline hemodynamic parameters were comparable in both groups. Group D had a reduction in HR from baseline starting from 2 min of loading dose infusion, and this decline persisted throughout the procedure. The reduction in the HR ranged from 5.3% at intubation and 8.8% at 10 min of MLScopy ($P = 0.001$), while placebo group showed significant rise in the HR from baseline and was found to be 21.3% at intubation to 18.2% at 10 min of MLScopy and remained elevated throughout the procedure and in the PACU [Table 2 and Figure 2].

During loading dose infusion, a rise in MBP was found at 2 min ($P = 0.018$) in Group D which was followed by a fall in MBP till induction. At intubation, both the groups showed a rise in MBP from baseline. However, on analyzing the magnitude of increase, patients in Group P exhibited a greater rise 16.7% in comparison to 5.2% rise in Group D ($P = 0.021$). Similarly, a greater rise in MBP from baseline was observed in placebo group throughout the procedure at all time points. At 10 min of MLscopy, the rise was 13.4% rise in placebo group against 0.1% rise index ($P = 0.002$). At the time of extubation also, MBP in Group D was found to be significantly lower than MBP in Group P [Table 3 and Figure 3].

Twelve patients (40%) in dexmedetomidine group and seven patients (23.3%) in placebo group were above the age of 50 with mean age of 54.875 in Group D, and 53.25 in Group P [Tables 4 and 5]. Three patients in Group P showed nonsignificant ECG changes which resolved spontaneously. No patient in Group D developed any ST-T changes. Bradycardia was observed in one patient in Group D. The HR dropped to 45/min, which responded to injection atropine 0.6 mg intravenously. Hypotension was not observed in any of the patients.

Table 1: Patient demographic and operative data

Variable	Mean±SD		Test applied	P
	Dexmedetomidine	Placebo		
Age (years)	43.7±13.0	37.7±13.8	Unpaired t-test	0.089
Weight (kg)	54.6±10.2	57.4±10.1	Unpaired t-test	0.285
ASA status	1.7±0.4	1.5±0.5	Unpaired t-test	0.111
Sex distribution				
Male	15	16	Fisher's exact test	1
Female	15	14		
Duration of microlaryngoscopy	14.7±5.4	15.6±8.5	Unpaired t-test	0.613

Expressed as mean±SD or absolute number. ASA=American Society of Anesthesiologists, SD=Standard deviation

Table 2: Variation in heart rate

	HR (/min)	Dexmed group		Placebo group		Test applied	P
		n	Mean±SD	n	Mean±SD		
Loading dose	0 min	30	90.9±14.0	30	84.3±18.0	Unpaired t-test	0.12
	2 min	30	88.9±16.7	30	82.3±14.9	Unpaired t-test	0.114
	10 min	30	80.4±16.3	30	81.9±14.0	Unpaired t-test	0.716
During microlaryngoscopy	At induction	30	79.2±13.5	30	81.0±15.0	Unpaired t-test	0.626
	At intubation	30	85.6±14.0	30	100.3±16.9	Unpaired t-test	0.01
	Postintubation	30	80.4±12.5	30	92.8±14.7	Unpaired t-test	0.001
	5 min	30	83.2±14.5	30	95.0±14.6	Unpaired t-test	0.003
	10 min	30	81.4±13.6	30	97.2±15.3	Unpaired t-test	0.01
	15 min	10	81.1±9.0	12	95.7±11.7	Unpaired t-test	0.004
	End of infusion	30	76.2±12.7	30	90.3±14.6	Unpaired t-test	0.01
	Extubation	30	77.0±12.3	30	88.1±12.5	Unpaired t-test	0.001
	Recovery	30	77.5±10.0	30	87.1±11.8	Unpaired t-test	0.003

Data expressed as mean±SD and P value. SD=Standard deviation, HR=Heart rate

**Table 3: Changes in mean blood pressure in both groups**

	MBP (mmHg)	Dexmed group		Placebo group		Test applied	P
		n	Mean±SD	n	Mean±SD		
Loading dose	0 min	30	89.5±10.7	30	86.2±7.0	Unpaired *t*-test	0.106
	2 min	30	90.1±9.7	30	84.6±7.3	Unpaired *t*-test	0.018
	10 min	30	84.3±8.8	30	85.5±7.0	Unpaired *t*-test	0.572
During microlaryngoscopy	At induction	30	86.4±8.4	30	82.8±7.3	Unpaired *t*-test	0.082
	At intubation	30	92.6±14.1	30	99.7±8.6	Unpaired *t*-test	0.021
	Postintubation	30	88.2±10.1	30	91.2±8.1	Unpaired *t*-test	0.21
	Before microlaryngoscopy	30	85.3±9.3	30	89.8±8.0	Unpaired *t*-test	0.047
	5 min	30	91.4±8.7	30	94.9±8.3	Unpaired *t*-test	0.124
	10 min	30	89.3±8.6	30	97±9.7	Unpaired *t*-test	0.002
	15 min	12	94±7.2	12	94.9±6.8	Unpaired *t*-test	0.751
	End of infusion	30	85.1±9.7	30	91.0±7.0	Unpaired *t*-test	0.008
	Extubation	30	85.8±10.0	30	87.7±7.5	Unpaired *t*-test	0.407
	Recovery	30	82.7±9.6	30	85.6±7.6	Unpaired *t*-test	0.321

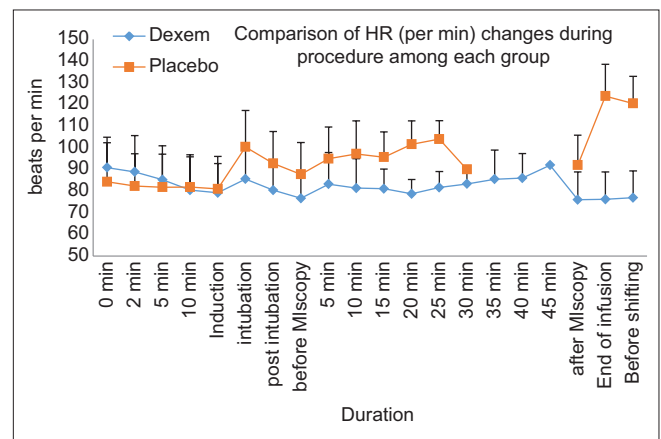*Data expressed as mean±SD and P value. MBP=Mean blood pressure, SD=Standard deviation*

Table 4: Variation in heart rate (above 50 years)

	HR (/min)	Dexmed group		Placebo group		Test applied	P
		n	Mean±SD	n	Mean±SD		
Loading dose	0 min	12	95.2±11.8	8	88±23.24	Unpaired *t*-test	0.29
	10 min	12	79.8±9.8	8	84±20.6	Unpaired *t*-test	
During microlaryngoscopy	At intubation	12	86.2±8.4	8	100±23.5	Unpaired *t*-test	0.20
	5 min	12	83.9±9.9	8	96±20.71	Unpaired *t*-test	0.18
	10 min	12	84.6±8.7	8	101±21.8	Unpaired *t*-test	0.06
	After microlaryngoscopy	12	77.6±6.4	8	89±19.2	Unpaired *t*-test	0.20
	Extubation	12	79.0±10.3	8	90±20.3	Unpaired *t*-test	0.19
	Recovery	12	82.7±9.9	8	88±18.2	Unpaired *t*-test	

Data expressed as mean±SD and P value. SD=Standard deviation, HR=Heart rate
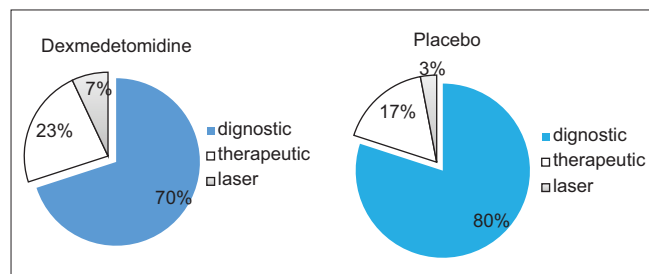
Figure 1: Type of surgery

Figure 2: Perioperative changes in heart rate

Fentanyl and propofol requirements to maintain hemodynamics within 20% of baseline values was found to be significantly reduced with dexmedetomidine. Only 2 (6.6%) patients in Group D against 11 (36.6%) patients in placebo group required fentanyl as rescue analgesic [Figure 4]. Meanwhile, propofol was required in only 1 (3.3%) patient in Group D and 9 (30%) patients in Group P. Total dose of fentanyl required was 52.5 ± 3.5 μg in Group D, whereas it was 70.9 ± 34.6 μg in Group P [Figure 5]. Total dose of propofol required was also found to be less (50 ± 0 mg) in dexmedetomidine group against (78.2 ± 29.5 mg) in control group.

The postoperative sedation scores 10 min' postextubation was comparable in both groups. Maximum patients in Group D were tranquil and responding to verbal commands (Ramsay sedation score [RSS] of 2 or 3) while in Group P 9 patients were agitated (RSS 1), and 2 patients showed RSS of 4. None of the patients experienced unpleasant memories or discomfort during anesthesia [Table 6].

Table 5: Changes in mean blood pressure in both groups (above 50 years)

	MBP (mm Hg)	Dexmed group		Placebo group		Test applied	P
		n	Mean±SD	n	Mean±SD		
Loading dose	0 min	12	89±9.8	8	87.0±7.0	Unpaired *t*-test	0.74
	10 min	12	83±9.2	8	84.4±7.2	Unpaired *t*-test	
During microlaryngoscopy	At intubation	12	94±11.2	8	101.1±12.4	Unpaired *t*-test	0.08
	Postintubation	12	86±11.0	8	90.9±8.7	Unpaired *t*-test	0.16
	5 min	12	88±10.0	8	94.3±10.5	Unpaired *t*-test	0.08
	10 min	12	89±10.2	8	97.0±12.7	Unpaired *t*-test	0.04
	End of infusion	12	82±12.9	8	92.8±6.4	Unpaired *t*-test	0.02
	Extubation	12	84±14.4	8	89.7±7.4	Unpaired *t*-test	0.13
	Recovery	12	81±10.3	8	89.3±6.7	Unpaired *t*-test	

Data expressed as mean±SD and P value. MBP=Mean blood pressure, SD=Standard deviation

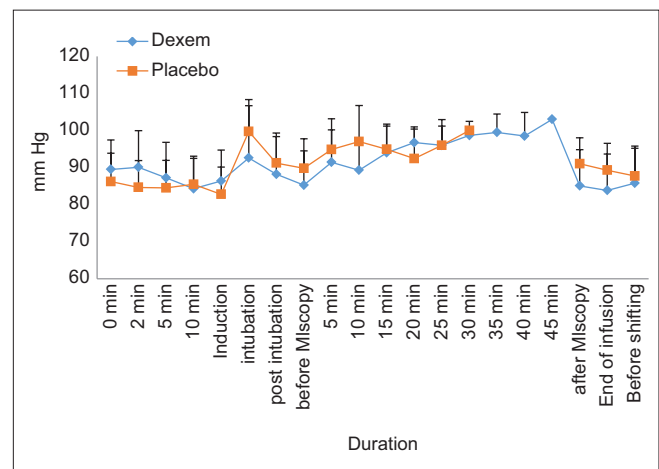**Table 6: Sedation score 10 min postextubation in both groups**

Ramsay sedation score	Response	Dexmed	Placebo
1	Anxious or restless or both	0	9
2	Cooperative, oriented and tranquil	25	15
3	Responding to verbal commands	5	4
4	Brisk response to stimulus	0	2
5	Sluggish response to stimulus	0	0
6	No response to stimulus	0	0

Data expressed as number

Figure 3: Perioperative changes in mean blood pressure

Discussion

MLScopy involves a series of stress-filled continuous suspension laryngoscopies leading to stimulation of deep pressure receptors of the larynx separated by varying periods of surgical stimulation.[2] Although patient population presenting for MLScopy are elderly, having a long history of heavy tobacco, alcohol use, and associated comorbidities that predispose them to respiratory and cardiovascular diseases. Uncontrolled hemodynamics in these patients can lead to fatal arrhythmias and myocardial ischemia.[5] Nevertheless, intraoperative procedure-related hypoxia, due to sharing of the common airway by surgeons and anesthetist may further accentuate the imbalance between myocardial oxygen supply and demand further aggravating arrhythmia, ischemia, and infarcts even in younger patients undergoing microlaryngeal surgery.[6] Strong *et al.* reported a tenfold higher incidence of cardiac complications such as myocardial infarction, transient ischemia, and significant arrhythmias after microsurgery of larynx.[7] Hence, a thoughtful consideration should be given by anesthesiologist to control perioperative cardiovascular stress responses to suspension laryngoscopy.

Various drugs such as propofol,[8,9] sevoflurane,[9] oral clonidine,[10] lignocaine spray,[2] β-blockers,[11] and oral gabapentin[12] have been used in various combinations and doses to ameliorate this hyperdynamic response to MLScopy.

However, a delayed postoperative awakening with propofol, delayed onset of action with oral clonidine and gabapentin and an increased incidence of complications secondary to myocardial depression with β-blockers were faced.

Intravenous dexmedetomidine, by causing 90% reduction in serum catecholamine levels, attenuates sympathoadrenal responses to intraoperative stress and intubation.[13,14] It has been effectively used for suppression of stress response during laryngoscopy and intubation.[15,16] Its anesthesia sparing,[16-18] opioid sparing action,[16,19] and blunting of exaggerated hemodynamic responses during surgery have also been documented.[20]

Our search did not find any study evaluating the efficacy of dexmedetomidine infusion on the suppression of hemodynamic responses to MLScopy. In the present study, we chose a loading dose of 1 μg/kg based on the literature,[13,14] followed by a continuous infusion to maintain constant plasma levels due to short distribution half-life (6 min) of dexmedetomidine.[14] Literature suggests that lower infusions of dexmedetomidine are associated with recall and recognition whereas higher doses cause bradycardia, hypertension, increased systemic, and pulmonary
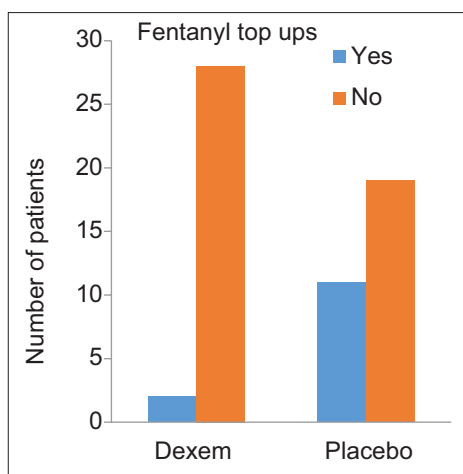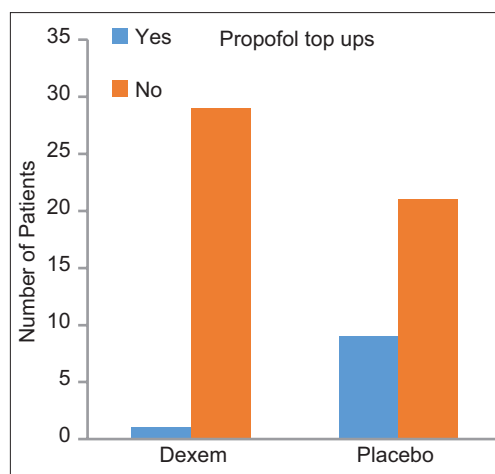
Figure 4: Perioperative fentanyl requirement

Figure 5: Perioperative propofol requirement

vascular resistance and a reduction in cardiac output.[14,21] Hence, a maintenance dose of 0.5 μ/kg/h which provides a linear kinetics was selected based on previous studies.[22,23]

Data of our study revealed that HR and MBP in Group D remained lower throughout the surgery than Group P. These hemodynamic effects can be attributed to the central sympatholytic action of dexmedetomidine.[13,14] It confirms the fact that critical incidences such as laryngoscopy and intubation, suspension laryngoscopy significantly accelerate the MBP and HR as seen in Group P and dexmedetomidine infusion attenuated the said exaggerated response. A transient increase in MBP was observed at 2 min of administration of dexmedetomidine infusion, which was followed by a fall probably due to the vasoconstriction effect of dexmedetomidine mediated by α2B receptors appearing before the central sympatholytic action.[13,14,20,21]

Perioperative stress during MLScopy can result in undesirable myocardial events. Dexmedetomidine modifies the stress response by reducing the release of stress hormones (norepinephrine, cortisol). Jianjun Ren *et al.* have evaluated this property of dexmedetomidine in patients of coronary artery disease undergoing off-pump coronary artery bypass (OPCAB). They witnessed a reduction in the levels of cardiac troponin I, creatine kinase-MB, norepinephrine, cortisol, BP, HR, myocardial ischemia, and postoperative arrhythmia with 0.2–0.5 μg/kg/h dexmedetomidine.[24] In the present study, none of the patients in Group D developed ST-T changes. The lower HR and BP in Group D could probably have resulted in reducing the myocardial oxygen demand and thus facilitating the maintenance of the myocardial oxygen supply and demand balance.

Intraoperatively, hemodynamics in Group D were well maintained and lesser mean dose and fewer number 2 (6.6%)

of patients required fentanyl as rescue analgesic in contrast to 11 (36.6%) patients in Group P. Similar findings have been described by Bajwa *et al.*[16] where patients in dexmedetomidine required lesser doses of fentanyl to maintain intraoperative hemodynamics. This could be due to the documented analgesic properties of dexmedetomidine.[18]

In the present study, end tidal concentration of sevoflurane was maintained at 2% throughout the procedure. Exaggerated hemodynamic response was attributed to inadequate depth of anesthesia due to unavailability of bispectral analysis (BIS)/entropy and was treated with a slow bolus of up to 1 mg/kg propofol. Propofol requirement to maintain hemodynamics was significantly reduced with dexmedetomidine exploring the anesthesia sparing properties of the drug. Bakhamees *et al.* also found a reduction in propofol requirement with dexmedetomidine in morbidly obese patients when propofol was used for maintenance of anesthesia using bispectral analysis (electroencephalogram) as the depth of anesthesia monitor.[17]

The study of time taken for extubation and quality of extubation was not a part of our study as laryngeal microscopic surgery leads to irritable airway due to mechanical trauma to laryngeal tissues, and hence extubation is sometimes delayed due to laryngeal edema. Ten percent lignocaine spray was found to be effective in suppression of cough response during extubation by Lee *et al.*[2] In the present study, lignocaine spray was used in all the patients to reduce airway irritation.

Smooth emergence and recovery from anesthesia is the goal for successful management of MLScopy.[25] Postoperative recovery of the patients was found to be better in Group D, could be due to anxiolytic, analgesic and anesthetic sparing properties of dexmedetomidine leading to improved recovery profile. Sedation produced by dexmedetomidine is like normal

sleep where patients are easily arousable and responding to verbal commands and then return to sleep like state when not stimulated.[14] In the placebo group, however, 9 (30%) patients were agitated whereas 2 patients had RSS of 4. This deeper level of sedation could be due to the excessive perioperative requirement of higher doses of other anesthetic drugs such as fentanyl and propofol.

The sympatholysis caused by dexmedetomidine has potential to increase the incidence of bradycardia and hypotension. Only one patient in the present study developed bradycardia in contrast to 3 patients in clonidine group as reported by Sunitha J Zachariah in their study of comparison of clonidine versus metoprolol for suppression of hemodynamic response to MLScopy.[11]

Conclusion

Dexmedetomidine, a novel α_2 agonist, is an excellent drug for attenuation of pressor response during intubation, during continuous airway manipulation as in microlaryngeal surgery. It has anesthetic and opioid sparing properties (lesser intraoperative propofol and fentanyl requirement) without causing delayed postoperative recovery.

Financial support and sponsorship

Conflicts of interest
There are no conflicts of interest.

References

1. Henderson J. Airway management in the adult. In: Miller RD, editor. Miller's Anesthesia. 7th ed. USA: Elsevier; 2010. p. 2560-618.
2. Lee DH, Park SJ. Effects of 10% lidocaine spray on arterial pressure increase due to suspension laryngoscopy and cough during extubation. Korean J Anesthesiol 2011;60:422-7.
3. Grewal A. Dexmedetomidine: New avenues. Indian J Anaesth 2011;27:297-302.
4. Chouhan Y, Parikh H. Effects of dexmedetomidine on hemodynamics in patients undergoing laparoscopic surgeries under general anaesthesia – A comparative study. Indian J Appl Res 2014;46:70-2.
5. Flory S, Appadurai IR. Special considerations in anesthesia for laryngeal cancer surgery. Otolaryngol Clin Int J 2010;2:185-90.
6. Michiels C. Physiological and pathological responses to hypoxia. Am J Pathol 2004;164:1875-82.
7. Strong MS, Vaughan CW, Mahler DL, Jaffe DR, Sullivan RC. Cardiac complications of microsurgery of the larynx: Etiology, incidence and prevention. Laryngoscope 1974;84:908-20.
8. Ebrahimi Dehkordi M, Razavi SS, Momenzadeh S. A comparison between sedative effect of propofol-fentanyl and propofol-midazolam combinations in microlaryngeal surgeries. Iran J Pharm Res 2012;11:287-94.
9. Bharti N, Chari P, Kumar P. Effect of sevoflurane versus propofol-based anesthesia on the hemodynamic response and recovery characteristics in patients undergoing microlaryngeal surgery. Saudi J Anaesth 2012;6:380-4.
10. Matot I, Sichel JY, Yofe V, Gozal Y. The effect of clonidine premedication on hemodynamic responses to microlaryngoscopy and rigid bronchoscopy. Anesth Analg 2000;91:828-33.
11. Zachariah SJ, Ninan S. Hemodynamic responses to microlaryngoscopy in ENT patients – A comparative study of premedication with oral clonidine and metoprolol. Int J Med Health Sci 2015;4:448-51.
12. Ayatollahi V, Mirshamsi P, Behdad S, Amirdosara M, Vaziribozorg S. Effect of oral gabapentin on haemodynamic variables during microlaryngoscopic surgery. Anaesthesiol Intensive Ther 2014;46:17-22.
13. Yazbek-Karam VG, Aouad MM. Perioperative uses of dexmedetomidine. Middle East J Anaesthesiol 2006;18:1043-58.
14. Afonso J, Reis F. Dexmedetomidine: Current role in anesthesia and intensive care. Rev Bras Anestesiol 2012;62:118-33.
15. Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian J Anaesth 2011;55:352-7.
16. Bajwa SJ, Kaur J, Singh A, Parmar S, Singh G, Kulshrestha A, *et al.* Attenuation of pressor response and dose sparing of opioids and anaesthetics with pre-operative dexmedetomidine. Indian J Anaesth 2012;56:123-8.
17. Bakhamees HS, El-Halafawy YM, El-Kerdawy HM, Gouda NM, Altemyatt S. Effects of dexmedetomidine in morbidly obese patients undergoing laparoscopic gastric bypass. Middle East J Anaesthesiol 2007;19:537-51.
18. Laha A, Ghosh S, Sarkar S. Attenuation of sympathoadrenal responses and anesthetic requirement by dexmedetomidine. Anesth Essays Res 2013;7:65-70.
19. Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, Ozcan B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Can J Anaesth 2006;53:646-52.
20. Kaymak C, Basar H, Doganci N, Sert O, Apan A. The effects of perioperative low – Moderate doses of dexmedetomidine infusion on hemodynamic and neuroendocrine parameters. Turk J Med Sci 2008;38:65-71.
21. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology 2000;93:382-94.
22. Rao SH, Sudhakar B, Subramanyam PK. Hemodynamic and anaesthetic advantages of dexmedetomidine. South Afr J Anaesth Analg 2012;18:326-31.
23. Kang WS, Kim SY, Son JC, Kim JD, Muhammad HB, Kim SH, *et al.* The effect of dexmedetomidine on the adjuvant propofol requirement and intraoperative hemodynamics during remifentanil-based anesthesia. Korean J Anesthesiol 2012;62:113-8.
24. Ren J, Zhang H, Huang L, Liu Y, Liu F, Dong Z. Protective effect of dexmedetomidine in coronary artery bypass grafting surgery. Exp Ther Med 2013;6:497-502.
25. Ahmed A, Saad D, Youness AR. Superior laryngeal nerve block as an adjuvant to general anesthesia during endoscopic laryngeal surgeries: A randomised controlled trial. Egypt J Anesth 2015;31:167-74.